## REMARKS

Claims 124-129 are pending in this application. Claims 1-123 have been canceled without prejudice or disclaimer in the Preliminary Amendment filed January 2, 2004. Applicants appreciate the previous acknowledgement, in the Office Action mailed June 23, 2006, that the elected species is allowable.

## The Rejection of Claims 124-129 under 35 U.S.C. § 103(a)

Claims 124-129 have been rejected under 35 U.S.C. § 103(a) as obvious over Raddatz et al. (AU 79823/87; "Raddatz"). Applicants respectfully traverse.

Claim 124 and its dependent claims 125-129 are directed to chiral amino alcohols of the formula

$$P^1 \longrightarrow N \longrightarrow N \longrightarrow N \longrightarrow N$$

wherein P1, P2, R2, and R3 are as defined in claim 124.

Page 3 of the Office Action asserts, "compounds overlapping applicants are generically disclosed [in Raddatz] where E is alkyl, the examples show E as H." However, neither alkyl nor H are possibilities for the group defined as "E" in Raddatz. In particular, "E" is -CONH-, -CONH-, -COO-, -SO<sub>2</sub>-, -SO<sub>2</sub>NH-, or -PO(OA)-O-. See the definition of "E" on page 2, lines 16-17 of Raddatz. In fact, not one of the extremely large number of compounds within the scope of generic formulas I, II, or III of Raddatz is also within the scope of the claimed compounds (i.e., there is no "overlap," as the Office Action alleges).

The Office Action cites the amino compounds of formula III on page 16. The most relevant of these have the formula III(b):

This genus of compounds cannot overlap the claimed compounds, at least because the right-hand "-E-Y" group cannot overlap any of the groups recited in the definition of R³ in the pending claims. See again the above definition for "E" as defined in Raddatz and also the particular examples given for the group -E-Y on page 3, lines 5-8.

Alternatively, the formula III(b) may be written as

The left-hand terminal nitrogen (which is substituted with  $R^4$ ) in the above formula is necessarily bound to at least one unsubstituted methylene carbon atom [ $-(CH_2)_n$ -, where n is 1 or 2]. See page 2, line 11 of Raddatz. In contrast, the claimed compounds require that the left-hand terminal nitrogen be bound to a substituted carbon atom, namely  $-CHR^2$ - ( $R^2$  is not hydrogen) as shown in generic formula for the chiral amino alcohols of claim 124. Again, overlap is not possible.

Finally, the Office Action points to the compound [S-(R\*,R\*] [3-amino-1-(cyclohexylmethyl)-2-hydroxypropyl] carbamic acid 1,1-dimethylethyl ester. For the reasons given in Applicants' response filed November 14, 2007, this compound is not within the scope of the pending claims. Nor is this compound within the scope of any of the formulas I, II, or III or Raddatz, as the Office Action implies. Consequently, the Office Action's assertion on page 3 is misplaced, namely that it would have been obvious

especially in view of close compounds already made, to make further disclosed compound[s] of formula III and expect them to be useful in making the title compounds of formula I. The allegedly "close compound" is not a compound of formula III or a "title compound" of formula I. Applicants searched through hundreds of compounds disclosed in Raddatz to find this "close compound" that the Office Action refers to is actually one of the starting materials used in Example 3. One having skill in the art would not have associated this compound with any particular significance in terms of biological activity, *let alone* have been motivated to modify this compound to arrive at the claimed compounds. Raddatz certainly contains no suggestion to do this.

Regarding obviousness of chemical compounds, the Federal Circuit recently held:

In addition to structural similarity between the compounds, a *prima facie* case of obviousness also requires a showing of "adequate support in the prior art" for the change in structure. *In re Grabiak*, 769 F.2d 729, 731-32 (Fed. Cir. 1985).

In order to find a prima facie case of unpatentability..., a showing that the "prior art would have suggested making the specific molecular modifications necessary to achieve the claimed invention" was also required. Id. (citing In re Jones, 958 F.2d 347 (Fed. Cir. 1992); Dillon, 919 F.2d 688; Grabiak, 769 F.2d 729; In re Lalu, 747 F.2d 703 (Fed. Cir. 1984)).

That test for prima facie obviousness for chemical compounds is consistent with the legal principles enunciated in KSR. . . . it remains necessary to identify some reason that would have led a chemist to modify a known compound in a particular manner to establish prima facie obviousness of a new claimed compound.

Takeda v. Alphapharm and Genpharm, 492 F.3d 1350, 1356-7 (Fed. Cir. 2007) (emphasis added). There is no reason why one of skill in the art would have considered it obvious to (i) choose a starting material from Raddatz, which is not even a compound of any of the formulas I, II, or III, taught in Raddatz to have biological activity (e.g., in the treatment of coronary, circulatory, and vascular disorders), and then (ii) modify this compound as required to obtain a compound within the scope of Applicants' claimed invention. Without any teaching or

suggestion in the art to make this proposed modification, the Office Action "can do no more than piece the invention together using the patented invention as a template. Such hindsight reasoning is impermissible." Texas Instruments Inc. v. U.S. ITC, 988 F.2d 1165, 1178 (Fed. Cir. 1993).

(2703/9/Div)

Raddatz does not render the invention of pending claims 124-129 obvious. Please withdraw the rejection under 35 U.S.C. § 103(a).

## CONCLUSION

Pending claims 124-129 of this application are in condition for allowance. Acknowledgement of the same is respectfully requested.

This response is believed to completely address all of the substantive issues raised in the Office Action dated June 13, 2008.

Respectfully submitted,

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